

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims

1-36 Cancel.

37. (new) A method of determining the activity of an enzyme, or the effect a test compound has on the activity of the enzyme, by using mass spectroscopy comprising the steps of:

- (i) providing a probe carrying an immobilised enzyme;
- (ii) optionally introducing the test compound;
- (iii) introducing one or more reactants to the immobilised enzyme for a time, and in a form sufficient for a reaction to take place;
- (iv) drying the probe;
- (v) subjecting the probe to mass spectroscopy;
- (vi) determining the activity of the enzyme, or the effect the test compound had on the activity of the enzyme, by detecting the presence and/or absence of one or more products and/or the one or more reactants;

characterised in that a layer resistant to non-specific protein binding is provided on the probe surface.

38. (new) The method of claim 37, wherein said layer resistant to non-specific protein binding comprises protein repellent molecules such as polyethylene glycol molecules, which protein repellent molecules are immobilised on the probe surface.

39. (new) The method of claim 37, wherein the enzyme is a kinase such as a serine kinase or threonine kinase, an oxidoreductase, a transferase, a hydrolase, a lyase, a ligase, a carboxylase, an esterase, a phosphodiesterase, a protein phosphatase such as a tyrosine phosphatase, a G-

protein coupled receptor, an ATP-dependent chaperone, a cyclooxygenase, a cytochrome P450, a sialidase, a short-chain dehydrogenase, a short-chain reductase, or an isomerase.

40. (new) The method of claim 37 for determining the activity of one or more kinases or the effect a test compound has on the activity of one or more kinases by using MALDI mass spectroscopy.

41. (new) The method of claim 40, wherein the one or more reactants comprise a phosphate donor, a phosphate acceptor and a divalent cation.

42. (new) The method of claim 41, wherein the phosphate donor is a phosphorylated substrate and the phosphate acceptor is a nucleotide di phosphate (NDP).

43. (new) The method of claim 41, wherein the phosphate donor is a nucleotide tri phosphate (NTP) and the phosphate acceptor is a substrate to be phosphorylated.

44. (new) The method of claim 41, wherein the divalent cation is magnesium or manganese.

45. (new) The method of claim 42, wherein the nucleotide di phosphate or tri phosphate is an adenine di or tri phosphate.

46. (new) The method of claim 37, wherein the product is a nucleotide tri phosphate or a nucleotide di phosphate and its presence is detected.

47. (new) The method of claim 46, wherein the nucleotide tri phosphate or nucleotide di phosphate are detected as $[\text{NDP}]^-$ or $[\text{NTP}]^-$ or as one or more adduct peaks thereof.

48. (new) The method as claimed in claim 47, wherein the one or more adduct peaks are adduct peaks with a monovalent cation (M^+).

49. (new) The method of claim 48, wherein the one or more adduct peaks include : [ATPM]⁻, [ATPM₂]⁻ and [ATPM₃]⁻ and/or [ADPM]⁻, [ADPM₂]⁻, and [ADPM₃]⁻.
50. (new) The method of claim 37, further comprising, between step (iv) and step (v), the step of overlaying the probe with energy absorbing molecules.
51. (new) The method of claim 50, wherein said energy absorbing molecules are deposited onto the probe surface in a non-aqueous solvent, followed by evaporation of the solvent.
52. (new) The method of claim 37, wherein said probe carries more than one enzyme.
53. (new) The method of in claim 37, wherein in step (iii) said one or more reactants are added in the presence of a low salt buffer.
54. (new) The method of claim 53, wherein said low salt buffer is a semi-volatile buffer such as ammonium bicarbonate buffer.
55. (new) The method of claim 37, wherein in step (iii) said one or more reactants are added in the presence of a buffer containing a semi-volatile salt; and further comprising the step, after the reaction is finished, of removing the semi-volatile buffer.
56. (new) The method of claim 37, wherein the enzymes are attached to the probe as fusion proteins, typically via a tag.
57. (new) The method of claim 37, wherein said test compound is added before, after or with the one or more reactants to determine its effect on enzyme activity.
58. (new) The method of claim 37, wherein the mass spectroscopy is a laser desorption ionisation mass spectroscopy, preferably a MALDI mass spectrometry.

59. (new) The method of claim 37, wherein the one or more reactants and the optional test compound are introduced to the immobilised enzyme as a droplet, such as a droplet having a volume of less than 1 microliter.

60. (new) A probe for use with a mass spectrometer in the method of claim 37, comprising a support having an electroconductive surface thereon, characterised in that the target surface comprises an array having a plurality of enzymes immobilised thereon, and in that the probe surface is provided with a layer resistant to non-specific protein binding.